

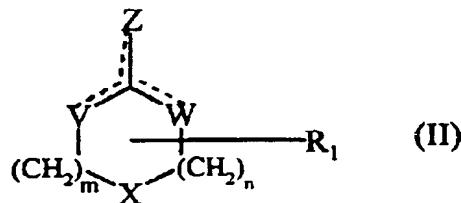
CLAIMS

✓. Compounds, in D, L or DL form, and salts thereof, of general formula (I):



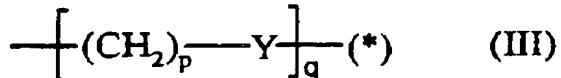
5 for which:

① CA represents a cycloamidine group and its mesomeric forms of general formula (II):



10 for which:

- m and n are integers, independent of each other, of between 0 and 3 inclusive and such that m+n is greater than or equal to 1,
- R<sub>1</sub> represents a group of general formula (III):



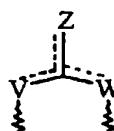
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for which p and q are integers, independent of each other, of between 0 and 10 inclusive, Y represents a carbonyl, amino, methylamino or methylene group, it being possible for Y to have different meanings within

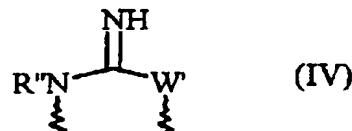
20 the different groups  $[(\text{CH}_2)_p - \text{Y}]$ , and (\*) represents either a hydrogen atom or is the site for bonding to the group Rep,

it being understood that  $R_1$  may be bonded to any atom of general formula (II), including  $Z$ , and that there is a single group  $R_1$  in formula (II),

- $X$  represents a group  $NR_2$  or  $CHR_2$ ,  $R_2$  being either a hydrogen atom or the bonding to the group  $R_1$  as defined above,

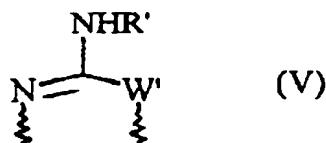
- The group  represents:

\*1st case: a group of general formula (IV) :



- 10 for which  $W'$  represents  $CHR_2$  or  $NR_2$ , and  $R''$  and  $R'$  represent, independently of each other, a hydrogen atom, a methyl, or the bonding to the group  $R_1$  as defined above, or

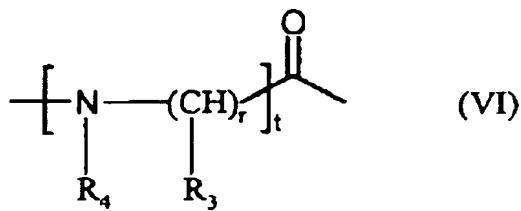
\*2nd case: a group of general formula (V) :



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- for which  $W'$  represents  $CHR_2$  or  $NR_2$ , and  $R'$  and  $R''$  represent, independently of each other, a hydrogen atom, a methyl or the bonding to the group  $R_1$  as defined above,

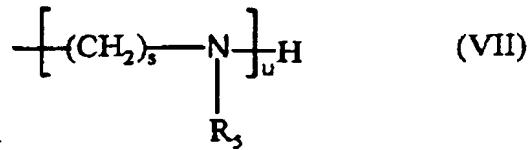
- 20 ② Rep is absent or is a spacer of general formula (VI) :



whose nitrogen atom is attached to the atoms X, V, W or Z or to the substituent Y of the group R<sub>1</sub> depending on the cases, and

- 5 • t is an integer between 0 and 8 inclusive,
- r is an integer between 0 and 10 inclusive, it being possible for r to have different meanings within the different groups -NR<sub>4</sub>- (CH)<sub>r</sub>-,
- R<sub>3</sub>, which may have different meanings within the

10 different groups NR<sub>4</sub>- (CH)<sub>r</sub>R<sub>3</sub>, represents a hydrogen atom, a methyl group or a group of general formula (VII):



for which u is an integer between 1 and 10 inclusive, s

15 is an integer between 2 and 8 inclusive which may have different meanings within the different groups - (CH<sub>2</sub>)<sub>s</sub>-NR<sub>5</sub>, and R<sub>5</sub> is a hydrogen atom, a group CA as defined above, it being understood that the groups CA are independent from each other and may be different,

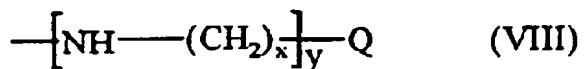
20 or a group of general formula (VII), it being understood that the groups of general formula (VII) are

independent of each other and may have different meanings,

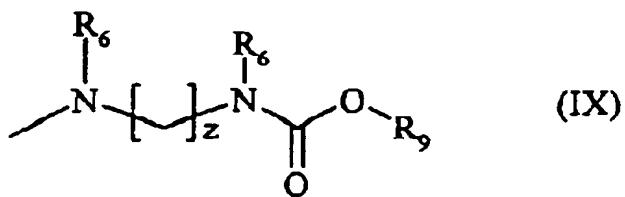
- R<sub>4</sub> is defined in the same manner as R<sub>3</sub> or represents a group CA as defined above, it being understood that the 5 groups CA are independent of each other and may be different, and

③ R is bonded to the carbonyl function of the group Rep of general formula (VI), or if Rep is absent, R is bonded directly to the group CA, and represents:

- 10 \* either a group of formula NR<sub>6</sub>R<sub>7</sub> for which R<sub>6</sub> and R<sub>7</sub> represent, independently of each other, a hydrogen atom or an optionally fluorinated, linear or branched, saturated or unsaturated aliphatic radical containing 1 to 22 carbon atoms, with at least one of the two
- 15 substituents R<sub>6</sub> or R<sub>7</sub> different from hydrogen and the other containing between 10 and 22 carbon atoms,
- \* or a steroid derivative,
- \* or a group of general formula (VIII) :



- 20 for which x is an integer between 1 and 8 inclusive, y is an integer between 1 and 10 inclusive, and either Q represents a group C(O)NR<sub>6</sub>R<sub>7</sub> for which R<sub>6</sub> and R<sub>7</sub> are as defined above, or Q represents a group C(O)R<sub>8</sub> for which R<sub>8</sub> represents a group of formula (IX) :



for which  $z$  is an integer between 2 and 8 inclusive, and  $R_9$  is an optionally fluorinated, saturated or unsaturated aliphatic radical containing 8 to 22 carbon atoms, or a steroid derivative, and the two substituents  $R_6$  are, independently of each other, as defined above,

or  $R_8$  represents a group  $-O-R_9$ , for which  $R_9$  is as defined above.

10 2. Compounds according to claim 1, characterized in that the group  $R_1$  is bonded either to  $Z$  or to  $V$ , on the one hand, and to the group Rep, on the other hand, via  $Y$ .

15 3. Compounds according to claim 1, characterized in that the cycloamidine head CA of formula (II) comprises 5, 6, 7 or 8 members.

20 4. Compounds according to claim 1, characterized in that  $R_3$  represents a hydrogen atom or a methyl and  $R_4$  is as defined in claim 1, or  $R_3$  and  $R_4$  present in formula (VI) represent hydrogen atoms, or  $R_4$  is a hydrogen atom and  $R_3$  is a group of formula (VII) in which  $R_5$  represents a group CA.

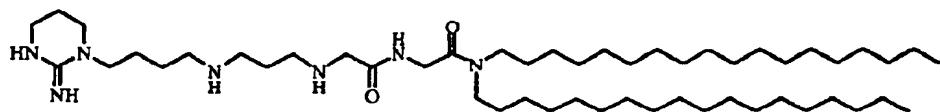
5. Compounds according to claim 1,  
characterized in that in formula (V), p and q are  
chosen, independently of each other, from 2, 3 or 4.

6. Compounds according to claim 1,  
5 characterized in that the groups R<sub>6</sub> and R<sub>7</sub> are identical  
or different and each represent optionally fluorinated,  
linear or branched, saturated or unsaturated aliphatic  
chains containing 10 to 22 carbon atoms.

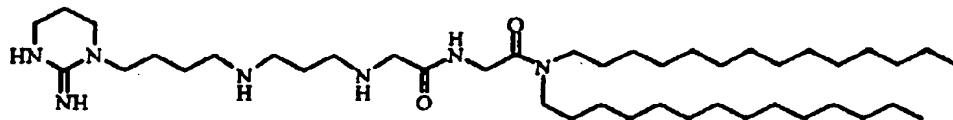
7. Compounds according to claim 1,  
10 characterized in that the groups R<sub>6</sub> and R<sub>7</sub> are identical  
or different and each represent optionally fluorinated,  
linear or branched, saturated or unsaturated aliphatic  
chains containing 12, 14, 16, 17, 18 or 19 carbon  
atoms.

15 8. Compounds according to claim 1,  
characterized in that when R is a steroid derivative,  
the said steroid derivative is chosen from cholesterol,  
cholestanol, 3- $\alpha$ -5-cyclo-5- $\alpha$ -cholest-6- $\beta$ -ol, cholic  
acid, cholesteryl formate, chotestanyl formate,  
20 3 $\alpha$ ,5-cyclo-5 $\alpha$ -cholest-6 $\beta$ -yl formate, cholesteryl-  
amine, 6-(1,5-dimethylhexyl)-3 $\alpha$ ,5 $\alpha$ -dimethylhexadeca-  
hydrocyclopenta[*a*]cyclopropa[2,3]cyclopenta[1,2-f]-  
naphthalen-10-ylamine or cholestanylamine.

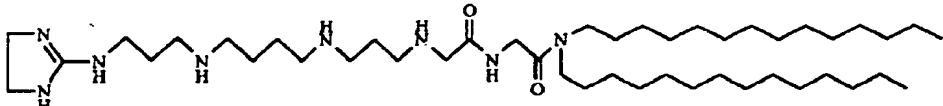
9. Compounds according to claim 1 of  
25 formulae:



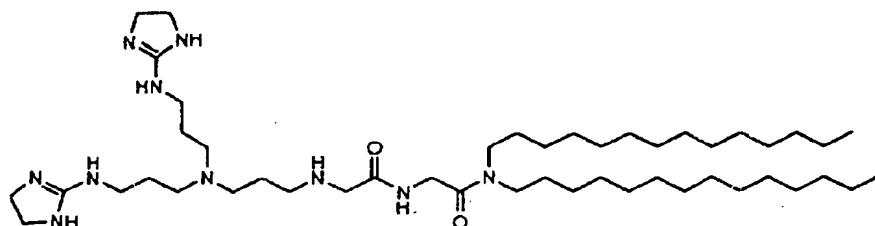
Compound (1)



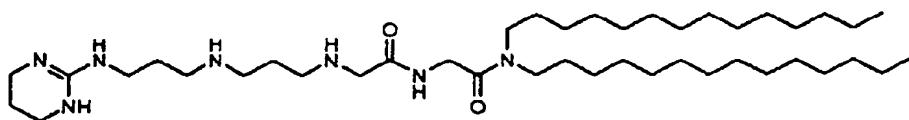
Compound (2)



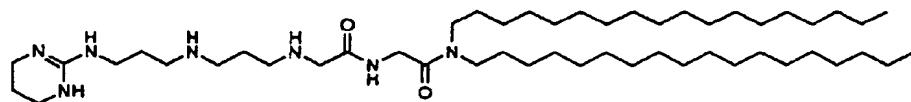
Compound (3)



Compound (4)



Compound (5)



Compound (6)

10. Method of preparing the compounds

according to claims 1 to 9, characterized in that the  
 15 synthesis of the building blocks carrying the  
 cycloamidine function(s) is carried out and then these

building blocks are grafted onto lipids equipped with spacers.

11. Method of preparing the compounds according to claims 1 to 8, characterized in that the 5 synthesis of the analogous lipopolyamines is carried out and then the cyclization into cycloamidine groups is carried out.

~~12.~~ Composition, characterized in that it comprises at least one compound of general formula (1).

10 13. Composition according to claim 12, characterized in that it comprises a compound of general formula (1) and a nucleic acid.

14. Composition according to claims 12 or 13, characterized in that it comprises, in addition, 15 one or more adjuvants.

15. Composition according to claim 14, characterized in that the adjuvant(s) are one or more neutral lipids containing two fatty chains.

16. Composition according to claim 15, 20 characterized in that the neutral lipids are natural or synthetic lipids which are zwitterionic or lacking ionic charge under physiological conditions, chosen for example from dioleoylphosphatidylethanolamine (DOPE), oleoylpalmitoylphosphatidylethanolamine (POPE), 25 di-stearoyl, -palmitoyl, -mirystoylphosphatidylethanol- amines as well as their derivatives which are N-methylated 1 to 3 times, phosphatidylglycerols,

diacylglycerols, glycosyldiacylglycerols, cerebrosides (such as in particular galactocerebrosides), sphingolipids (such as in particular sphingomyelins) or asialogangliosides (such as in particular asialoGM1 and 5 GM2).

17. Composition according to claim 14, characterized in that the adjuvant is a compound involved directly or otherwise in the condensation of the nucleic acid.

10 18. Composition according to claim 17, characterized in that said adjuvant is derived as a whole or in part from a protamine, a histone or a nucleolin and/or from one of their derivatives, or consists, as a whole or in part, of peptide units 15 (KTPKKAKKP) and/or (ATPAKKAA), it being possible for the number of units to vary between 2 and 10, and to be repeated continuously or otherwise.

19. Composition according to claims 12 to 18, characterized in that it contains, in addition, one 20 or more nonionic surfactant(s) in a sufficient quantity to stabilize the size of the particles of nucleolipid complexes.

20. Composition according to claims 12 to 19, characterized in that it comprises a vehicle which 25 is pharmaceutically acceptable for an injectable formulation.

21. Composition according to claims 12 to 19, characterized in that it comprises a vehicle which is pharmaceutically acceptable for an application to the skin and/or the mucous membranes.

5 22. Composition according to claim 13, characterized in that the said nucleic acid is a deoxyribonucleic acid or a ribonucleic acid.

23. Composition according to claim 22, characterized in that the said nucleic acid comprises 10 an expression cassette consisting of one or more gènes of therapeutic interest under the control of one or more promoters and of a transcriptional terminator which are active in the target cells.

24. Use of a compound according to one of 15 claims 1 to 9, to manufacture a medicament for treating diseases.

25. Use of a compound according to one of claims 1 to 9, to manufacture a medicament for treating diseases by transfer of nucleic acids into cells by the 20 intramuscular route.

~~26. Method of transferring nucleic acids into cells comprising the following steps:~~

- (1) bringing the nucleic acid into contact with a compound of general formula (1) as defined above, to 25 form a nucleolipid complex, and
- (2) bringing the cells into contact with the nucleolipid complex formed in (1).

27. Method of transferring nucleic acids into cells according to claim 26, characterized in that the said nucleic acid and/or the said compound are previously mixed with one or more adjuvants.

5 28. Method of treating diseases by administration of a nucleic acid encoding a protein or which can be transcribed into a nucleic acid capable of correcting the said diseases, the said nucleic acid being combined with a compound of general formula (I).